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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 11/26/2002

28

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action SummaryApplication No.
09/392,822Applicant(s)
Yu et al.Examiner
Joseph WeitachArt Unit
1632**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --****Period for Reply**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Aug 27, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 8, 14-16, 21, 24-26, and 32-46 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 8, 14-16, 21, 24-26, and 32-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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DETAILED ACTION

This application filed September 9, 2000, claims benefit to provision application filed September 10, 1999.

Applicants' amendment filed August 27, 2002, paper number 26, has been received and entered. The specification has been amended. Claims 14-16, 21, 40 and 41 have been amended. Claims 1, 8, 14-16, 21, 24-26 and 32-46 are pending and currently under examination.

Specification

The disclosure objected to because of sequence requirements is withdrawn.

The substitute sequence listing and the amendments to the specification have obviated the basis of the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-16, 21 and 38-40 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn.

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Applicants note that multiple examples of regulatory elements specifically contemplated and encompassed by the term TRE are described in the present disclosure. Further, it is noted that the specification discusses properties of the types of promoters contemplated, and in particular, the properties of TREs which would be useful in the context of the instant invention. Applicants argue that in light of the teachings of the present disclosure and in view of the level of skill and knowledge in the art, the present specification meets the requirements for written description as required under 35 USC 112, first paragraph. See Applicants' amendment, page 4. Applicants' arguments have been fully considered and found persuasive.

Upon consideration Applicants' arguments and upon review of the specification and the art of record, Examiner agrees that the present specification meets the written description requirements of 35 USC 112, first paragraph. Specifically, the requirement of written description has been met by the disclosure of a number of specific promoters encompassed by the term TRE, the general discussion of TRE promoter activity, and the general knowledge of one of skill in the art for identifying and characterizing promoters.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 8, 14-16, 21, 24, 26 and 40 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

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Amendments to the claims have obviated the basis of each of the specific rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 8, 14-16, 21, 25, 26 and 32-46 stand rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Henderson *et al.* (WO 97/01358) Hallenbeck *et al.* (WO 96/17053), Walther *et al.* (Mol. Biotechnol., 6:267-286), Dachs *et al.* (Nat. Med., 3(5):515-520), Dachs *et al.* (Oncol. Res., 9:313-325), Advani *et al.* (Semin. Oncol., 24(6):633-638), and Parr *et al.* (Nat. Med., 3(10):1145-1149).

Applicants summarize the teachings of each of the cited references, specifically noting embodiments each reference fails to teach. Further, Applicants note that Examiner acknowledges that none of the references teach a hypoxia responsive element which is now required in the amended claims. See Applicants' amendment, pages 5-6. Applicants' arguments have been fully considered and found persuasive.

First, it is important to note that in the basis of the previous rejection the teaching of Walther *et al.* was specifically discussed in review of the state of the art concerning targeted vectors for gene therapy of cancer and discloses several types of cell status-specific TREs

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including those comprising a hypoxia responsive elements and heat-inducible elements (see e.g. “Tumor Therapy-Inducible Gene Therapy” section pages 279-281) (see previous office action top of page 12). Therefore, it is noted that each of the limitations encompassed by the claims are present in the cited references. With respect to Applicants comments and arguments, Examiner agrees with the summary of each of the separate references, however the courts have stated that arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, Examiner acknowledges the deficiencies of each of the references, however the teaching and combination of the teaching of each of the references must be viewed as a whole. The courts have held that the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Further, for the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. *In re Nilssen*, 7 USPQ2d 1500 (Fed. Cir. 1988). In the instant case, each of the limitations encompassed by the instant claims are taught in the cited references. The motivation and reasons for combining the teachings were discussed in detail in the previous office action, relying on specific motivation in the references themselves and sound scientific reasoning. As summarized in the previous office action,

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Henderson and Hallenbeck each teach adenovirus vectors which comprise cell specific TREs and propose the use of these vectors to affect various treatments. Walther, Dachs, Advani, and Parr are relied upon for the teaching of specific promoters and each teach and provide the motivation of the benefits of combining tumor specific, cell type specific, and/or cell status-specific regulatory elements in the context of various vectors. Thus, it is maintained that at the time the invention was made it would have been *prima facie* obvious to one of ordinary skill in the art to substitute or combine methods the cell type specific TREs in the conditionally replication-competent adenovirus vectors of Henderson and Hallenbeck with the cell status-specific TREs disclosed by Walther, Dachs, Advani, or Parr, since each Walther, Dachs, and Advani teach the benefits of combining tumor specific, cell type specific, and/or cell status-specific regulatory elements. Additionally, one would have been motivated to substitute other specific promoters since the art teaches and supports the use of cell status specific regulatory elements are inducible by well-established treatments, e.g. radiation and hypothermia, and that operably linkage to radiation-inducible, heat-inducible, hypoxia-inducible or cell cycle-inducible regulatory elements (comprising cell status-specific TREs) allows for more effective and selective transgene expression and tumor eradication with significantly less normal tissue toxicity than seen with standard adenoviral vectors.

Finally, though not specifically argued by Applicant, it is noted that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988). In the instant case, given the level of skill in the art for generating polynucleotide vectors,

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there is a reasonable expectation that the artisan can combine the various vector elements to produce the vectors encompassed by the instant claims.

Thus, for the reasons above and of record, the invention was *prima facie* obvious at the time the invention was made, and therefore, the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

Claims 14-16 and 21 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 8, and 32 of copending Application No. 09/151,376 is withdrawn.

Amendments to the claims have differentiated the present claims from those set forth in Application No. 09/151,376.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach



DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/630